concentration." Claim 1 has been amended to recite that the claimed nucleic acid molecule is "purified" and that it "comprises a mammalian Hypertension-Related Calcium-Regulated Gene (HCaRG)." These amendments to claim 1 are supported by the specification which discloses that "the present inventors describe the isolation and characterization of a novel gene, designated *HCaRG*." (Page 4, lines 15-16.) Claims 3-5 have also been amended to recite nucleic acids that are "purified." These amendments are also supported at this citation in the specification.

Claims 2 and 6 are each dependent on claim 1 and have been amended to recite "The nucleic acid as defined in claim 1" in place of "A nucleic acid as defined in claim 1." This amendment merely corrects a formal matter and does not narrow the scope of the claims.

Claim 6 has been amended to recite dependency on claim 1, and claims 8 and 15 have been amended recite dependency on claim 24.

Claim 11 has been amended to recite the nucleic acid of at least 12 nucleotides in length "hybridizes to nucleic acids of a calcium sensing cell" in place of is "capable of a specific hybridization to nucleic acids of a calcium sensing cell." The amendment is supported by the specification which discloses how to hybridize probes to nucleic acid sequences in cells. The specification discloses that "[h]ybridization was performed by adding the probe." (Page 33, lines 27-28.) This amendment also does not narrow the scope of the claim.

Claims 12 and 13 are each dependent on claim 11 and have been amended to correct the antecedent basis of "nucleic acid." This amendment merely corrects a formal matter and does not narrow the scope of the claims.

Claim 16 has been amended to refer to the nucleic acids of claim 25, in place of claim 6. The nucleic acid of claim 25 is an *HCaRG* nucleic acid that encodes SEQ ID NO: 4. The

specification, which discloses that SEQ ID NO: 4 is encoded by the human *HCaRG* nucleic acid, supports this amendment. (Page 4, line 30 through page 5, line 5.)

New claim 24 is directed to a purified nucleic acid that comprises *HCaRG*, wherein the *HCaRG* encodes SEQ ID NO: 2. New claim 25 is directed to a purified nucleic acid that comprises *HCaRG*, wherein the *HCaRG* encodes SEQ ID NO: 4. Claims 24 and 25 are supported by the specification which discloses that

> the present invention relates to a nucleic acid molecule isolated from parathyroid of a mammal and whose expression is regulated by extracellular calcium concentration. In one case, the mammal is a human and the molecule encodes the amino acid sequence set out in Figure 4 (bottom lines). In another case, the mammal is a rat and the molecule encodes the amino acid sequence set out in Figure 4 (top lines).

Page 4, line 30 through page 5, line 2. The human amino acid sequence shown in Figure 4 is SEQ ID NO: 4. The rat amino acid sequence shown in Figure 4 is SEQ ID NO: 2.

New claim 26 is directed to a recombinant vector that comprises the nucleic acid molecule of claim 25. The nucleic acid molecule of claim 25 encodes SEQ ID NO: 4. New claim 26 is supported by originally filed claim 7, which is directed a recombinant vector that comprises *HCaRG*. New claim 26 is also supported by the specification which discloses that human *HCaRG* encodes SEQ ID NO: 4. (Page 5, lines 1-2.)

New claim 27 is directed to a recombinant host cell that comprises the recombinant vector of claim 26. The recombinant vector of claim 26 comprises a nucleic acid sequence that encodes SEQ ID NO: 4. Claim 27 is supported by originally filed claim 9 which is directed to a recombinant host cell containing a recombinant vector which comprises an *HCaRG* nucleic acid

molecule. Claim 27 is also supported by the specification which discloses that human *HCaRG* encodes SEQ ID NO: 4. (Page 5, lines 1-2.)

New claim 28 is directed to a composition of matter that comprises the recombinant vector of claim 25 and a carrier. The recombinant vector of claim 25 comprises a purified *HCaRG* that encodes SEQ ID NO: 4. Claim 28 is supported by originally filed claim 17 which is directed to a composition of matter that comprises a recombinant vector comprising an *HCaRG* and a carrier. Claim 28 is also supported by the specification which discloses that human *HCaRG* encodes SEQ ID NO: 4. (Page 5, lines 1-2.)

New claim 29 is directed to a composition of matter that comprises the recombinant host cell of claim 27 and a carrier. The recombinant host cell of claim 27 comprises a recombinant vector containing an *HCaRG* nucleic acid that encodes SEQ ID NO: 4. Claim 29 is supported by originally filed claims 22 and 23 which are directed to compositions of matter comprising recombinant host cells containing recombinant vectors that comprise *HCaRG* nucleic acids and the specification which discloses that human *HCaRG* encodes SEQ ID NO: 4. (Page 5, lines 1-2.)

The specification has also been amended at the paragraph that begins on page 4 at line 30. The amendment corrects an inadvertent error in which the amino acid sequence encoded by rat *HCaRG* is described as being the bottom sequence of the alignment disclosed in Figure 4. Figure 4 supports this amendment. The top sequence in Figure 4 is indicated as being "rHCaRG."

None of these amendments introduces new matter.

The Rejection of Claims 1-6, 11, 14-16, and 19 Under 35 U.S.C. § 101

Claims 1-6, 11, 14-16, and 19 have been rejected under 35 U.S.C. § 101 for being directed to non-statutory subject matter. This rejection is respectfully traversed.

The Office Action asserts that the rejected claims are directed to non-statutory subject matter because they recite nucleic acid sequences that read on products of nature. Independent claims 1 and 11, and dependent claims 3-5 have been amended to recite that the claimed nucleic acid molecules are "purified." Thus amended independent claims 1 and 11 and dependent claims 2-6, 14-16, and 19 are directed to statutory subject matter. Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 1, 3-5, 7-14, and 16-23 Under 35 U.S.C. § 112, first paragraph

Claims 1, 3-5, 7-14, and 16-23 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not sufficiently described in the specification. The rejection is respectfully traversed.

To comply with the written description requirement, the description must clearly convey to persons of ordinary skill in the art that applicants invented what is claimed. *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). The subject matter of the claim need not be described literally (*in haec verba*) for the disclosure to satisfy the written description requirement. See MPEP § 2163.02. The disclosure of the instant application conveys to one of skill in the art that applicants invented what is claimed.

Claims 1, 3-5, 7-10, 14, 16-18, 22, and 23

The Office Action asserts that the specification does not adequately describe a genus of

nucleic acid molecules "isolatable from the parathyroid of a mammal and whose expression is regulated by extracellular calcium concentration," as recited in originally filed claim 1. (Office at page 3, second paragraph.) Claim 1, however, has been amended and now recites a genus of nucleic acid molecules "comprising a mammalian Hypertension-Related Gene (*HCaRG*)." The written description requirement for a genus of nucleic acid molecules

> may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

The Regents of the University of Calfornia v. Eli Lilly and Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997). See also MPEP § 2163. The specification meets this requirement.

First, the specification discloses a representative number of *HCaRG* nucleic acids. The specification discloses the sequences of rat *HCaRG* (SEQ ID NO: 1) and human *HCaRG* (SEQ ID NO: 3). These sequences are representative of the genus of *HCaRG* nucleic acid molecules because they share a high degree of identity. "Sequence comparison between human *HCaRG* and rat *HCaRG* showed 80% identity at the nucleotide level (data not presented) and, similarly, 80% homology at the amino acid level." (Page 22, lines 16-18.) Thus the specification discloses a representative number of species in the genus of *HCaRG* nucleic acids.

Second, the specification discloses structural features common to members of the *HCaRG* genus. Figure 4 shows an alignment of the amino acid sequences encoded by the rat and human *HCaRG*s. The

> analysis [of the rat and human *HCaRG*s] revealed homology to the EF-hand motif, with 8 out of the 10 most conserved amino acids (dashed box). Further analysis using the PROSEARCH database revealed 4 overlapping putative 'leucine zipper' consensus motifs

(underlined). We also identified a nuclear receptor-binding domain (bold and italics).

Page 9, lines 28-31. Thus the specification also discloses structural features common to members of the *HCaRG* genus.

The rejection of claims 8, 10, 16, 18, and 23 also cannot stand. Claims 8, 10, 18, and 23 are directed to recombinant vectors, recombinant host cells, and compositions of matter that comprise *HCaRG* molecules that encode the amino acid sequence of SEQ ID NO: 2. New claim 24 is directed to a purified nucleic acid molecule that encodes SEQ ID NO: 2. The disclosure of SEQ ID NO: 2 is sufficient to demonstrate that applicants had possession of the *HCaRG* molecules recited in claims 8, 10, 18, 23, and new claim 24.

> Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species. Cf. *In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).

MPEP § 2163(II)(A)(3)(a)(ii). Thus one of skill in the art would readily recognize that applicants possessed the genus of nucleic acid molecules encoding SEQ ID NO: 2. For the same reasons, no written description rejection should apply to claim 16 or to new claims 25-28, which recite nucleic molecules encoding SEQ ID NO: 4.

Claims 11-13 and 19-21

The specification also demonstrates that applicants had possession of the nucleic acids recited in claims 11-13 and 19-21. The Office Action also asserts that "the specification does not disclose any sequences within SEQ ID NO: 1 and 3 that would allow for specific hybridization of probes as recited in originally filed claim 11." (Office Action, page 3, lines 13-14.) Claim 11,

however, has been amended to recite a purified nucleic acid that "hybridizes to nucleic acids" with the sequence of SEQ ID NO: 1, SEQ ID NO: 3 or complementary sequences thereof. The specification discloses the nucleotide sequences of SEQ ID NO: 1 and SEQ ID NO: 3. The base pairing rules for hybridization are well known. Thus, a disclosure of SEQ ID NO: 1 and SEQ ID NO: 3 also is a disclosure of their complementary sequences. Any nucleic acid at least twelve nucleotides in length of the complement of SEQ ID NO: 1 or SEQ ID NO: 3 is a member of the genus recited in claims 11-13 and 19-21. Similarly, any nucleic acid at least 12 nucleotides in length of SEQ ID NO: 1 or SEQ ID NO: 3 is a member of the genus of such a nucleic acid that hybridizes to the complementary sequence of SEQ ID NO: 1 or SEQ ID NO: 3. A person of skill in the art would not expect substantial variation among other species encompassed within the scope of the claims because the nucleic acids that hybridize over any particular stretch of at least twelve nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, or a complementary sequence thereof is expected to be structurally similar, owing to their ability to hybridize with the recited sequences. Thus, the disclosure of the nucleic acid sequences of SEQ ID NO: 1 and SEQ ID NO: 3 is sufficient to demonstrate that applicants were in possession of nucleic acids recited in claims 11-13 and 19-21.

Withdrawal of this rejection to claims 1, 3-5, 7-14, and 16-23 is respectfully requested.

The Rejection of Claims 2-6 and 11-13 Under 35 U.S.C. § 112, second paragraph

Claims 2-6 and 11-13 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is respectfully traversed.

The Office Action asserts that claims 2-6, 12, and 13 are unclear because they do not recite proper antecedent basis for elements referred to in the claims from which they depend. Claims 2, 5, 6, 12, and 13 have been amended to correct this deficiency. Claims 3 and 4 have not been amended because they recite "the nucleic acid of claim 2" and thus are believed to recite proper antecedent basis from claim 2.

The Office Action also asserts that claims 11-13 are unclear because the phrase "specifically hybridizes" is indefinite. The Office Action alleges that applicants have not provided the conditions for specific hybridization, thus rendering the metes and bounds of the claims undeterminable. Independent claim 11 has been amended to recite a nucleic acid that "hybridizes" to nucleic acids of a calcium sensing cell in place of is "capable of a specific hybridization" with the nucleic acids. Thus the allegedly indefinite characteristic of the hybridization conditions has been removed and the deficiency has been corrected.

Withdrawal of these rejections to claims 2-6 and 11-13 is respectfully requested.

The Objection to Claim 1

Claim 1 has been objected to because isolatable is incorrectly spelled as "isolable." Claim 1 has been amended and no longer recites isolatable. Thus the objection is rendered moot. Withdrawal of this objection is respectfully requested.

Respectfully submitted,

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Appendix I. Marked-Up Version of the Claims and Specification to Show the Changes Made

Claims

1. (Amended) A purified nucleic acid molecule [isolable from parathyroid of a mammal and whose expression is regulated by extracellular calcium concentration, or its complementary strand] comprising a mammalian Hypertension-Related Calcium-Regulated Gene (HCaRG).

2. (Amended) [A] The nucleic acid molecule as defined in claim 1, having the sequence set out in SEQ ID No. 1, or its complementary strand.

3. (Amended) A purified nucleic acid molecule, having an homology of at least 60% with the nucleic acid of claim 2.

4. (Amended) A purified nucleic acid molecule, having an homology of at least 80% with the nucleic acid of claim 2.

5. (Amended) [A] The purified nucleic acid molecule as defined in claim 4, wherein the mammal is a human.

6. (Amended) [A] The nucleic acid as defined in claim [5] 1, which has the sequence set out in SEQ ID No. 3.

8. (Amended) A recombinant vector comprising the nucleic acid of claim [5] 24.

11. (Amended) A purified nucleic acid of at least 12 nucleotides in length [capable of a specific hybridization with the] that hybridizes to nucleic acids of a calcium sensing cell and with SEQ ID No. 1, SEQ ID No. 3, or a complementary sequence thereof.

12. (Amended) [A] The nucleic acid as defined in claim 11 which is an amplification primer.

13. (Amended) [A] The nucleic acid as defined in claim 11, which is a hybridization probe.

15. (Amended) A composition of matter comprising the nucleic acid of claim [5] 24 and a carrier.

16. (Amended) A composition of matter comprising the nucleic acid of claim [6] 25 and a carrier.

Specification

The paragraph beginning on page 4, line 30 and ending on page 5, line 5.

Therefore the present invention relates to a nucleic acid molecule isolated from parathyroid of a mammal and whose expression is regulated by extracellular calcium concentration. In one case, the mammal is a human and the molecule encodes the amino acid sequence set out in Figure 4 (bottom lines). In another case, the mammal is a rat and the molecule encodes the amino acid sequence set out in Figure 4 ([bottom] top lines). The invention includes a nucleotide molecule of a human, and having a homology of 60% or greater to all or part of the sequence set out in Figure 1. The molecule may have a 60% or greater homology to the translated portion of the sequence.